

PRELIMINARY AMENDMENT
U.S. Appln. No. 10/612,090

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions and listings of claims in the application:

LISTING OF CLAIMS:

1. (Original) An isolated monoclonal antibody that specifically binds to an epitope of a non-shed extracellular portion of a shed antigen.
2. (Original) An isolated monoclonal antibody that specifically binds to an epitope of a non-shed extracellular portion of human Muc1 or Muc16 protein.
3. (Original) A hybridoma that produces the antibody of claim 1 or 2.
4. (Original) The antibody of claim 1 or 2, wherein said antibody is selected from the group consisting of a recombinant antibody, a fragment of a recombinant antibody, a humanized antibody, and an antibody displayed upon the surface of a phage.
5. (Original) The antibody of claim 1 or 2, wherein said antibody is prepared using a non-shed extracellular portion of the antigen attached to an immunogenic protein carrier.
6. (Original) The antibody of claim 1 or 2, wherein said antibody is produced by immunization of an animal with a recombinant fusion protein comprising an extracellular non-shed portion of the antigen.
7. (Original) The antibody of claim 6, wherein said fusion protein is a glutathione-S-transferase fusion protein.
8. (Original) The antibody of claim 1 or 2, wherein said antibody is produced by immunization of an animal with a cell expressing a recombinant non-shed extracellular portion of the antigen.
9. (Original) The antibody of claim 2, wherein at least a part of said epitope is located within the carboxy-terminal 90 amino acids of the extracellular domain of Muc1.

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10. (Original) The antibody of claim 9, wherein at least a part of said epitope is located within the amino acid sequence:

FLQIYKQGGFLGLSNIKFRPGSVVVQLTLAFREGTINVHDTVETQFNQYKTE
AASRYNLTISDVSVDVPPFSAQSGAGVPGWGIA (SEQ ID NO: 1).

11. (Original) The antibody of claim 10, wherein said antibody binds to at least one peptide selected from the group consisting of:

- a) QLTLAFREGTINVHDTVETQFN (SEQ ID NO:8);
- b) QYKTEAASRYNLTISDVSVD (SEQ ID NO:9);
- c) FLQIYKQGGFLGLSNIKFRPG (SEQ ID NO:10);
- d) FRPGSVVVQLTLAFREGTINV (SEQ ID NO:11); and
- e) VPPFSAQSGAGVPGWGIA (SEQ ID NO:12).

12. (Original) The antibody of claim 2, wherein at least a part of said epitope is located within the carboxy-terminal 110 amino acids of the extracellular domain of Muc16.

13. (Original) The antibody of claim 12, wherein at least a part of said epitope is located within the amino acid sequence:

TNYQRNKRNIEDALNQLFRNSSIKSYFSDCQVSTFRSVPNRHHTGVDSL CNFSPL
ARRVDRVAIYEEFLRMTRNGTQLQNFTLDRSSVLVDGYSPNRNEPLTGNSDLP
(SEQ ID NO:2).

14. (Original) The antibody of claim 13, wherein said antibody binds to at least one peptide selected from the group consisting of:

- a) SSVLVDGYSPNRNEPLTGNS (SEQ ID NO:14);
- b) TNYQRNKRNIEDALNQLFRN (SEQ ID NO:15);
- c) FRNSSIKSYFSDCQVSTFRSV (SEQ ID NO:16);
- d) SVPNRHHTGVDSL CNFSPLARRV (SEQ ID NO:17); and
- e) DRVAIYEEFLRMTRNGTQLQNFTLDRSS (SEQ ID NO:18).

15. (Original) A conjugate comprising an antibody of claim 1 or claim 2 attached to a cytotoxic agent or a prodrug of a cytotoxic agent.

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16. (Original) The conjugate of claim 15, wherein said cytotoxic agent is a small drug.
17. (Original) The conjugate of claim 15, wherein said cytotoxic agent is a maytansinoid, taxoid, or CC-1065 analog.
18. (Original) A composition comprising the antibody of claim 1 or claim 2 and a pharmaceutically acceptable carrier.
19. (Original) A composition comprising the conjugate of claim 15 and a pharmaceutically acceptable carrier.
20. (Original) A method of treating a subject in need thereof, comprising administering to said subject an effective amount of the composition of claim 18.
21. (Original) A method of treating a subject in need thereof, comprising administering to said subject an effective amount of the composition of claim 19.
22. (Original) The method of claim 20, wherein said subject has a cancer.
23. (Original) The method of claim 21, wherein said subject has a cancer.
24. (Original) The method of claim 22, wherein said cancer is a cancer wherein Muc1 or Muc16 is overexpressed.
25. (Original) The method of claim 23, wherein said cancer is a cancer wherein Muc1 or Muc16 is overexpressed.
26. (Original) A method for screening a subject suspected of having a cancer, comprising
 - (a) providing a sample of a tissue from said subject;
 - (b) measuring the amount of a non-shed extracellular portion of a shed antigen in said sample using the antibody of claim 1; and
 - (c) comparing the amount of said antigen to the amount of said antigen in cancerous and non-cancerous controls, whereby the screening of said subject is performed.
27. (Original) The method of claim 26, wherein the antigen is human Muc1 or Muc16.

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28. (Original) The method of claim 26 or 27, wherein said cancer is ovarian cancer or breast cancer.

29. (Original) A method of screening for an antibody that specifically binds to a non-shed portion of a surface antigen, said method comprising:

(a) measuring binding of a candidate antibody to a cell expressing the antigen on its surface;

(b) measuring binding of said candidate antibody to fragments of said antigen shed from said cell into an extracellular medium; and

(c) comparing the binding measurements of step (a) and step (b), whereby said antibody is screened.

30. (Original) The method of claim 29, wherein the surface antigen is Muc1 or Muc16.

31. (Currently Amended) An isolated monoclonal antibody MJ-170 produced by hybridoma cell line MJ-170 on deposit with the American Type Culture Collection (ATCC) as accession number ~~HB~~ PTA-5286.

32. (Currently Amended) An isolated monoclonal antibody MJ-171 produced by hybridoma cell line MJ-171 on deposit with the ATCC as accession number ~~HB~~ PTA-5287.

33. (Currently Amended) An isolated monoclonal antibody MJ-172 produced by hybridoma cell line MJ-172 on deposit with the ATCC as accession number ~~HB~~ PTA-5288.

34. (Currently Amended) An isolated monoclonal antibody MJ-173 produced by hybridoma cell line MJ-173 on deposit with the ATCC as accession number ~~HB~~ PTA-5302.

35. (Currently Amended) A hybridoma cell line MJ-170 on deposit with the ATCC as accession number ~~HB~~ PTA-5286.

36. (Currently Amended) A hybridoma cell line MJ-171 on deposit with the ATCC as accession number ~~HB~~ PTA-5287.

37. (Currently Amended) A hybridoma cell line MJ-172 on deposit with the ATCC as accession number ~~HB~~ PTA-5288.

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38. (Currently Amended) A hybridoma cell line MJ-173 on deposit with the ATCC as accession number ~~HB~~ PTA-5302.

39. (Original) An antibody that is a functional equivalent of the monoclonal antibody of claim 31, 32, 33 or 34, wherein said antibody is selected from the group consisting of a monoclonal antibody, a recombinant antibody, a single chain antibody, a chimeric antibody, a humanized antibody, a CDR-grafted antibody, an antibody displayed on the surface of a phage and an antibody fragment thereof.

40. (Original) A conjugate comprising an antibody of claim 31, 32, 33 or 34, attached to a cytotoxic agent or a prodrug of a cytotoxic agent.

41. (Original) The conjugate of claim 40, wherein said cytotoxic agent is a small drug.

42. (Original) The conjugate of claim 40, wherein said cytotoxic agent is a maytansinoid, a taxoid, or a CC-1065 analog.

43. (Original) A composition comprising an antibody of claim 31, 32, 33 or 34 and a pharmaceutically acceptable carrier.

44. (Original) A composition comprising the conjugate of claim 40 and a pharmaceutically acceptable carrier.

45. (Original) A method of treating a subject in need thereof, comprising administering to said subject an effective amount of the composition of claim 43.

46. (Original) A method of treating a subject in need thereof, comprising administering to said subject an effective amount of the composition of claim 44.

47. (Original) The method of claim 45, wherein said subject has a cancer.

48. (Original) The method of claim 46, wherein said subject has a cancer.

49. (Original) The method of claim 47, wherein said cancer is a cancer wherein Muc1 or Muc16 is overexpressed.

50. (Original) The method of claim 48, wherein said cancer is a cancer wherein Muc1 or Muc16 is overexpressed.